

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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WASHINGTON, DC 20043-9998

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

01 APR 2005

Applicant's or agent's file reference

2240-203461

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US04/13756

International filing date (day/month/year)

05 May 2004 (05.05.2004)

Priority date (day/month/year)

05 May 2003 (05.05.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 48/00; C12N 15/74 and US Cl.: 514/44; 435/320.1

Applicant

JOHNS HOPKINS UNIVERSITY

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

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Authorized officer

Q. Janice Li

Telephone No. 703-308-0196

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/13756

Box No. 1 Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☒ in written format

☒ in computer readable form

c. time of filing/furnishing

☒ contained in international application as filed.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/13756

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO
Inventive step (IS)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO
Industrial applicability (IA)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO

2. Citations and explanations:

Claims 1-9, 11, 12, 15, 16, 18-20, 22-24, 26-29, 31-33, 35-37, 39, 40 lack an inventive step under PCT Article 33(3) as being obvious over Gajewczyk et al in view of Chen et al.

Gajewczyk et al teach DNA vaccine vectors encoding non-toxic (non-oncogenic) HPV-E6/E7 and using such for treating cervical cancer. They teach that mice immunized with the DNA vaccine remained tumor free up to 90 days after tumor inoculation (e.g. examples 5-10). Gajewczyk et al do not teach including hsp70 in the DNA vaccine regime.

Chen et al supplemented Gajewczyk et al by establishing that it is well known in the art that hsp70 could enhance DNA vaccination against viral and cancer antigen. *Chen et al* teach that heat shock protein 70 (hsp70) could enhance the vaccine effect of a DNA vector expressing an antigenic viral protein (e.g. JEV), and suggested co-administration of plasmid pHSP70 with a plasmid DNA encoding tumor or viral-specific antigens.

Although Chen et al do not teach making a construct comprising both the hsp70 and an antigen, given the knowledge of the skill, it would have been obvious to one of the skilled in the art to either co-administering two vectors expressing both hsp70 and an antigen, or making a construct comprising both an antigen and a hsp70. The skilled would have been motivated to do so for enhanced effect of HPV vaccination. Thus, the claimed invention as a whole was prima facie obvious in the absence of evidence to the contrary.

Claims 10, 13, 14, 17, 21, 25, 30, 34, 38 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the amino acid substitutions of SEQ ID Nos: 2 & 4 as indicated in claims 10 and 11.

Claims 1-40 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/13756

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

V.1. Reasoned Statements:

The opinion as to Novelty was positive (Yes) with respect to claims 1-40

The opinion as to Novelty was negative (No) with respect to claims NONE

The opinion as to Inventive Step was positive (Yes) with respect to claims 10, 13, 14, 17, 21, 25, 30, 34, 38

The opinion as to Inventive Step was negative (NO) with respect to claims 1-9, 11, 12, 15, 16, 18-20, 22-24, 26-29, 31-33, 35-37, 39, 40

The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-40

The opinion as to Industrial Applicability was negative (NO) with respect to claims NONE

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 2240-203461	FOR FURTHER ACTION <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/US04/13756	International filing date (<i>day/month/year</i>) 05 May 2004 (05.05.2004)	(Earliest) Priority Date (<i>day/month/year</i>) 05 May 2003 (05.05.2003)
Applicant JOHNS HOPKINS UNIVERSITY		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).



- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box No. II)

3. ☐ Unity of invention is lacking (See Box No. III)

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. ____



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.



- b. none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/13756

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material

☒

a sequence listing

☐

table(s) related to the sequence listing

b. format of material

☒

in written format

☒

in computer readable form

c. time of filing/furnishing

☒

contained in the international application as filed

☒

filed together with the international application in computer readable form

☐

furnished subsequently to this Authority for the purposes of search

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/13756

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 48/00; C12N 15/74

US CL : 514/44; 435/320.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/44; 435/320.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Sequence databases, EAST, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6,235,523 (GAJEWCZYK ET AL) 22 MAY 2001. See abstract for example.	1-9, 11, 12, 15, 16, 18-20, 22-24, 26-29, 31-33, 35-37, 39, 40
Y	CHEN, W. ET AL: Modulatory effects of the human heat shock protein 70 on DNA vaccination. See e.g. the last sentence of the abstract.	1-9, 11, 12, 15, 16, 18-20, 22-24, 26-29, 31-33, 35-37, 39, 40
T — A	US 6,734,173 B1 (WU ET AL) 11 MAY 2004 See for example claims 1-3 and SEQ ID Nos: 2, 9, 22.	1-9, 11, 12, 15, 16, 18-20, 22-24, 26-29, 31-33, 35-37, 39, 40 10, 13, 14, 17, 21, 25, 30, 34, 38

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

16 March 2005 (16.03.2005)

Date of mailing of the international search report

01 APR 2005

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